METHOD AND APPARATUS FOR SORTING PARTICLES

RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 13/158,960, filed Jun. 13, 2011 and entitled "METHOD AND APPARATUS FOR SORTING PARTICLES," which is a continuation of U.S. patent application Ser. No. 12/537,802, filed Aug. 7, 2009, which is a continuation of U.S. patent application Ser. No. 11/499,953, filed Aug. 7, 2006, which is a continuation of U.S. patent application Ser. No. 10/940,143 entitled "Method and Apparatus for Sorting Particles" filed Sep. 13, 2004, which is a divisional of U.S. patent application Ser. No. 10/179,488 entitled "Method and Apparatus for Sorting Particles" filed Jun. 24, 2002 which claims priority to U.S. Provisional Patent Application Ser. No. 60/373,256 entitled "Microfluidic System Including a Bubble Valve for Regulating Fluid Flow Through a Microchannel" filed Apr. 17, 2002, the contents of each application is incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

The invention relates to a method and apparatus for the sorting of particles in a suspension, where the input flow path of a sorting module can be split into several output channels. More particular, the invention relates to a particle sorting system in which a plurality of sorting modules are interconnected as to yield an increased particle throughput.

BACKGROUND OF THE INVENTION

In the fields of biotechnology, and especially cytology and drug screening, there is a need for high throughput sorting of particles. Examples of particles that require sorting are various types of cells, such as blood platelets, white blood cells, tumorous cells, embryonic cells and the like. These particles are especially of interest in the field of cytology. Other particles are (macro) molecular species such as proteins, enzymes and poly-nucleotides. This family of particles is of particular interest in the field of drug screening during the development of new drugs.

Methods and apparatuses for particle sorting are known, and the majority described in the prior art work in the condition where the particles are suspended in a liquid flowing through a channel network having at least a branch point downstream and are operated according the detect-decide-deflect principle. The moving particle is first analyzed for a specific characteristic, such as optical absorption, fluorescent intensity, size etc. Depending on the outcome of this detection phase, it is decided how the particle will be handled further with. The outcome of the decision is then applied to deflect the direction of specific particle towards a predetermined branch of the channel network.

Of importance is the throughput of the sorting apparatus, i.e. how many particles can be sorted per unit of time. Typical sorting rates for sorters employing flows of particle suspension in closed channels are in the range from a few hundred particles per second to thousands of particles per second, for a single sorting unit.

An example of a sorting device is described in U.S. Pat. No. 4,175,662, the contents of which are herein incorporated by reference. In the '662 patent, a flow of particles, cells in this case, flows through the center of a straight channel, which branches into two perpendicular channels at a branching point downstream (T-branch). The entering particles are surrounded by a sheath of compatible liquid, keeping the particles confined to the center of the channel. In normal conditions, the flow ratio through the two branches is adjusted so that the particles automatically flow through one of the branches. In a section of the channel a characteristic of the particles is determined using a detector, which can be an optical system (detection phase). The detector raises a signal, which is interpreted. When the detector detects a particle possessing a predetermined characteristic in the decision phase, a deflector is activated for deflecting the particle in a deflection phase. In this case, the deflector comprises an electrode pair, positioned in the branch of the channel where the particles normally flow through in the inactivated state of the deflector. By the application of current pulses, the aqueous liquid is electrolysed, yielding a gas bubble evolving between the electrode pair. As the gas bubble increases in size, the flow rate through this branch is reduced during the evolving phase. After the current pulse is applied, the bubble growth stops and the gas bubble is carried along with the flow. As a result, the flow through the specific branch is momentarily reduced and the particle of interest changes paths and flows down the other branch.

The described device is effective for sorting particles, however one serious drawback is that gas bubbles are created which potentially can accumulate at certain points of the fluidic network or clog flow channels, yielding erroneous sorting. Another drawback is that the generated gasses (mostly oxygen and hydrogen) and ionic species (mostly OH^- and H^+) influence the particles flowing through the branch with the electrode pair. In addition, cells and delicate proteins such as enzymes are very fragile and can be destroyed by the fouling constituents co-generated with the gas bubble. Another drawback is the complexity of the overall sorting apparatus. In particular, the micro electrode construction is very complex to mount and assemble in the small channels of the system. As a result, the cost of a sorting unit is relatively large.

Another example of a particle sorting system of the prior art is disclosed in U.S. Pat. No. 3,984,307, the contents of which are herein incorporated by reference. In the '307 patent, the particles are flowing, confined by a flowing sheath liquid, through the center of a channel. After passing a detector section, the channel branches to two channels under an acute angle (Y-branch). Just before the branching point, an electrically activated transducer is located in the channel for deflecting a specific particle having an appropriate, predetermined characteristic. The transducer described is a piezo actuator or ultrasonic transducer, yielding upon electrical activation a pressure wave in the channel. The generated pressure wave momentarily disturbs the flow in one branch thus deflecting the particle of interest into the other branch

Also in this device, as in the previous discussed device, the deflector is incorporated within the channel system, resulting in relatively large costs of construction. Another drawback is the deflector principle used. The generated pressure waves are not confined to the branching point, but will propagate upstream into the detector section as well as downstream both branches and influence the overall flow through the channel. This is particularly a drawback if sorters of this type are connected either in series or in parallel as to build a sorter system with increased throughput. Pressure waves generated in one sorter can then influence the flows and deflection of particles in neighboring sorter units.